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(54) Title: TREATMENT WITH CYTOKINES

(57) **Abstract:** An inflammatory process is suggested to be involved in the pathogenesis of Alzheimer's disease (AD), a neurode-  
generative disorder characterized by the presence of neuritic plaques within the cerebral cortex that are mainly composed of a small  
insoluble protein of 40-42 aminoacids (amyloid protein). The biological correlates of this process are nevertheless not clear. In-  
terleukin-10 (IL-10) is a cytokine that suppresses T lymphocytes and cell-mediated immunity in humans and mice and has potent  
anti-inflammatory properties. To verify if IL-10 production would be impaired in AD patients we stimulated PBMC of 47 patients  
and 25 age-matched healthy controls (HC) with a mitogen, a recall antigen or with amyloid peptides. IL-2 production was measured  
as well in the same cultural conditions. Results showed that amyloid-specific IL-10 generation is selectively and significantly re-  
duced in AD patients ( $p=0.023$ ). Analyses on the alleles of the IL-10 gene revealed that the genotype associated with high IL-10  
production is extremely infrequent in AD individuals (2% vs. 28%). The presence of low/intermediate IL-10-producing genotypes  
(GCC/ATA; ATA/ATA) was associated with an earlier age at disease onset and (ACC/ACC; ACC/ATA) with an accelerated rate of  
disease progression. These data shed light on the biology of the inflammatory process involved in the pathogenesis of AD by show-  
ing that the presence of low-IL-10-allelic isoforms results in an amyloid-specific impairment of IL-10 production and is associated  
with the clinical severity of AD. These results lend support to the use of anti-inflammatory compounds in the therapy of this disease.

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